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Pharmaceuticals, Inc.

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20850

April 30,1999

Ref: Docket No. 99D-0236
Draft Guidance for Industry:
Skin Irritation and Sensitization Testing of
Generic Transdermal Drug Products

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Dear Sir/Madam:

Boehringer Ingelheim Pharmaceuticals, Inc. has reviewed the FDA draft guidance on "Skin Irritation and Sensitization Testing of Generic Transdermal Drug Products", and is taking this opportunity to provide comments on the guidance.

We applaud the Agency's efforts in developing a guidance to assist sponsors of transdermal drug abbreviated new drug applications. The draft guidance clearly lays out the current regulatory thinking for evaluating the skin irritation and sensitization potential of generic transdermal systems. While we believe that the document has been carefully developed and that most of the recommendations are appropriate, we as an ethical pharmaceutical company that has developed and marketed a transdermal product for the past 15 years, offer the following comments for your consideration.

The guidance should give some recommendations for the choice of the subjects. Experience in marketing a once-a-week system for the past 13 years has been that women of Northern European lineage are more susceptible to skin irritation and sensitization than other female ethnic groups and males. In the Cumulative Skin Irritation Study we recommend that a substantial number of the study participants (one third or greater) be women of Northern European lineage to obtain statistical power in the study.

Secondly, we recommend that either the lowest dose possible of the active drug substance be used in the two study designs if normal volunteers are recruited or that the dose be titrated to the proper therapeutic level if patients are recruited. While it is important that potential skin irritation and sensitization be studied

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with both drug and excipients together in these study designs, care should be taken to ensure the safety of the subjects.

We commend the Agency for its efforts to develop this guidance and would welcome the opportunity to further discuss the Agency issues pertaining to skin irritation and sensitization following transdermal drug delivery in general or to our comments in general.

Sincerely,

Kathryn M. Jason, Ph.D
Sr. Associate Director,
Drug Regulatory Affairs

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